

DISERTASI

ANALISIS PERBEDAAN MIKROBIOTA SALURAN Cerna BERBASIS METAGENOMIK DAN HUBUNGANNYA DENGAN STRES OKSIDATIF PADA NEONATUS PREMATUR DAN CUKUP BULAN



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ABSTRAK

ANALISIS PERBEDAAN MIKROBIOTA SALURAN Cerna BERBASIS METAGENOMIK DAN HUBUNGANNYA DENGAN STRES OKSIDATIF PADA NEONATUS PREMATUR DAN CUKUP BULAN

Latar Belakang : Prematuritas meningkatkan risiko stres oksidatif dan mengganggu kolonisasi awal mikrobiota saluran cerna akibat ketidakmatangan berbagai sistem organ. Hubungan antara profil mikrobiota saluran cerna dan stres oksidatif pada neonatus masih belum banyak diteliti. Penelitian ini bertujuan membandingkan profil mikrobiota saluran cerna berbasis metagenomik dan biomarker stres oksidatif antara neonatus prematur dan cukup bulan serta menganalisis hubungan keduanya.

Metode: Penelitian analitik observasional dengan desain *cross-sectional* komparatif dilakukan pada 25 neonatus yang terdiri atas 14 neonatus prematur dan 11 neonatus cukup bulan. Sampel mekonium digunakan untuk pemeriksaan kadar AOPP dan MDA menggunakan metode ELISA serta analisis metagenomik gen 16S rRNA regio V3-V4 menggunakan platform Illumina MiSeq. Analisis bioinformatika dilakukan menggunakan Cutadapt, DADA2, phyloseq, dan basis data SILVA 138.2. Analisis meliputi kelimpahan relatif, *alpha diversity*, *beta diversity* dan hubungan antara mikrobiota saluran cerna dengan biomarker stres oksidatif.

Hasil: Kelompok neonatus cukup bulan didominasi oleh genus *Escherichia-Shigella*, sedangkan neonatus prematur memiliki kelimpahan relatif *Klebsiella* dan *Staphylococcus* yang lebih tinggi. Tidak terdapat perbedaan signifikan pada *alpha diversity*. Analisis *beta diversity* menunjukkan perbedaan komposisi mikrobiota yang signifikan berdasarkan Bray-Curtis ($R^2 = 0,146$; $p = 0,002$) dan Jaccard ($R^2 = 0,117$; $p = 0,004$). Kadar AOPP dan MDA lebih tinggi pada neonatus prematur dibandingkan neonatus cukup bulan. Genus *Orrella* merupakan satu-satunya takson yang berhubungan signifikan dengan biomarker stres oksidatif.

Kesimpulan: Prematuritas berhubungan dengan mikrobiota saluran cerna dan peningkatan stres oksidatif sejak awal kehidupan. Genus *Orrella* merupakan taksa yang berhubungan dengan kadar AOPP. Mekonium berpotensi menjadi spesimen noninvasif untuk analisis metagenomik dan biomarker stres oksidatif pada neonatus.

Kata kunci : AOPP, MDA, mekonium, metagenomik, mikrobiota saluran cerna, prematuritas, stres oksidatif

ABSTRACT

METAGENOMIC DIFFERENCES ANALYSIS IN THE GUT MICROBIOTA AND THEIR ASSOCIATION WITH OXIDATIVE STRESS IN PRETERM AND TERM NEONATES

Background: Prematurity increases the risk of oxidative stress and disrupts the early colonization of the gut microbiota because of the immaturity of multiple organ systems. However, the relationship between gut microbiota composition and oxidative stress in neonates remains poorly understood. This study compared metagenomic gut microbiota profiles and oxidative stress biomarkers between preterm and term neonates and examined the association between gut microbiota composition and oxidative stress.

Methods: This comparative cross-sectional observational study included 25 neonates, comprising 14 preterm and 11 term neonates. Meconium samples were collected for the measurement of advanced oxidation protein products (AOPP) and malondialdehyde (MDA) using enzyme-linked immunosorbent assay (ELISA) and for 16S rRNA gene metagenomic sequencing targeting the V3 to V4 region on the Illumina MiSeq platform. Bioinformatic analyses were performed using Cutadapt, DADA2, phyloseq, and the SILVA 138.2 reference database. Analyses included relative abundance, alpha diversity, beta diversity, and associations between gut microbiota and oxidative stress biomarkers.

Results: The gut microbiota of term neonates was predominantly composed of the genus *Escherichia-Shigella*, whereas preterm neonates showed higher relative abundances of *Klebsiella* and *Staphylococcus*. No significant difference was observed in alpha diversity between the two groups. Beta diversity analysis demonstrated significant differences in microbial community composition based on the Bray-Curtis ($R^2 = 0.146$, $p = 0.002$) and Jaccard ($R^2 = 0.117$, $p = 0.004$) distance metrics. AOPP and MDA concentrations were higher in preterm than in term neonates. The genus *Orrella* was the only taxon significantly associated with oxidative stress biomarkers.

Conclusion: Prematurity was associated with gut microbiota composition and increased oxidative stress during early life. The genus *Orrella* was associated with AOPP concentrations. Meconium shows promise as a noninvasive specimen for metagenomic analysis and the assessment of oxidative stress biomarkers in neonates.

Kata kunci : AOPP, gut microbiota, MDA, meconium, metagenomics, oxidative stress, prematurity.